REMARKS

Claims 1, 5-12, 17, 19-22, 25, 29-35 and 37 are all the claims pending in the application. Claims 5, 7-10, 17, 19-22, 29, and 31-34 are withdrawn as being directed to a non-elected invention. Claims 1, 6, 11, 12, 25, 30 and 37 are being examined. Claims 5-12 and 29-34 have been amended to remove dependency from canceled claims and to correct the spelling of galectin-3. The preamble of claim 25 has been amended for purposes of clarity only to recite a method of therapy or preventive treatment, rather than a method of inhibiting a disease. Claim 37 has been added to correspond to previously presented claim 36. Claim 36 was rejected in the prior Office Action only because it depended from claim 25, which was alleged to be indefinite and non-enabled. Since claim 37 depends from claim 25, no new issue of patentability is raised if claim 25 is found allowable. Accordingly, entry of the amendment is requested, respectfully.

Objection Withdrawn

In paragraph No. 4 at page 2 of the Office Action, the Examiner has withdrawn the previous objection of claims 6 and 11 in view of the amendment and response dated May 27, 2003.

Rejections Withdrawn

In paragraph No. 5 at page 2, the Examiner has withdrawn the previous rejection of claims 1-4, 6, 11, and 12 under 35 U.S.C. § 112, first paragraph in view of the amendment and response dated May 27, 2003.

In paragraph No. 6 at page 2, the Examiner has withdrawn the previous rejection of claims 1-4, 6, 11, 12, 25, 27, 30, 35, and 36 under 35 U.S.C. § 112, second paragraph in view of the amendment and response dated May 27, 2003.

Rejection Under 35 U.S.C. § 112, first paragraph

In paragraph No. 7 at page 3, the Examiner rejected claims 1, 3, 6, 11, 12, 25, 30, and 35 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement in the specification. While recognizing that the specification enables in relation to a pharmaceutical composition comprising an identified compound such as LNFP-1 and fetuin, the Examiner alleged that the specification does not provide enabling disclosure for compositions comprising compounds other than LNFP-1 and fetuin.

In particular, the Examiner maintained the positions asserted in the previous Office Action that:

(1) The specification does not establish a correlation between *in-vitro* data and the *in-vivo* effect; and

(2) The specification does not teach all possible compounds having inhibitory activity on galectin-3 as claimed.

For the following reasons, the rejection is traversed.

The present invention functions as follows:

(a) Inhibition of galectin-3,

↓

(b) Repression of ECM over-production/accumulation,

↓

(c) Therapeutic or preventive action on glomerular nephritis.

Enablement of the functioning of the invention is supported as disclosed below:

Step (a)

Substances that inhibit galectin-3 can be found as described in Examples 5 and 6 of the present application. Example 5 describes a method for testing for inhibitory activity of "fetuin glycoprotein" against galectin-3. Example 6 describes a method for testing for inhibitory activity of "lacto-n-fucopentaose" against galectin-3. These methods can be applied to test any test substance in place of the fetuin glycoprotein or lacto-n-fucopentaose. It is only necessary to measure the amount of type IV collagen produced. From the results, it can be determined whether or not the test substance can inhibit galectin-3.

Thus, although the specification does not name every possible inhibitor, substances that inhibit galectin-3 can be selected easily from candidate substances by one of ordinary skill in the art by applying conventional screening methods, such as those described in Examples 5 and 6.

Furthermore, at pages 6-8 of the specification, applicants identify six types of compounds that one of ordinary skill in the art can look to for candidates and expect to be successful. That is, there is guidance as to where to find suitable compounds. Therefore the specification is broadly enabling for inhibitors of galectin-3.

Step (a) to (b)

Example 4 shows that galectin-3 promotes the production of type IV collagen, which is an extracellular matrix (ECM), by type IV collagen-producing cells. In addition, Examples 5

and 6 show that substances that inhibit galectin-3 repress the promotion by galectin-3 of the production and accumulation of the type IV collagen in the type IV collagen-producing cells. Therefore, it is clear that any substance that inhibits galectin-3 represses the promotion by galectin-3 of the production and accumulation of ECM from ECM-producing cells. It is believed that the Examiner does not dispute this.

Step (b) to (c)

The Examiner asserted that the application does not show a correlation between the production and accumulation of ECM and glomerular nephritis.

In responding to this issue raised in the last Office Action, applicants pointed out that it is well known in the art that an accumulation of extracellular matrix causes the diseases recited in the claims, namely, glomerular nephritis, diabetic nephropathy and tissue fibrosis. The present invention is based on the discovery by the present inventors that galectin-3 promotes the accumulation of extracellular matrix. Therefore, it is reasonable to expect that a substance that inhibits the activity of galectin-3 would also be suitable to treat glomerular nephritis, diabetic nephropathy and tissue fibrosis.

Applicants further pointed out that the relationship between the accumulation of ECM and various diseases is already described in the specification and applicants submitted three references (two authored by Shimizu, *et a*l. and one by and Al-Bayati *et al.*) which demonstrated a correlation between the overproduction of collagen and alleviation of renal diseases.

The Examiner was unpersuaded by these three references.

Accordingly, submitted herewith are two additional references demonstrating a correlation between the accumulation of ECM and diseases and the ability to alleviate symptoms of the diseases by inhibiting accumulation of collagen.

Rastaldi et al., Kidney International, Vol. 62 (2002), p. 137 - 146 (Reference 1) (submitted herewith) analyzes human kidney samples to study the relationship between the extracellular matrix and glomerular nephritis. Reference 1 reports that in comparison to a healthy kidney, a kidney having glomerular nephritis over-expresses collagen, which is a component of the ECM. (See, the section "RESULTS" and Table 2 of Reference 1)

Huang et al., The Journal of Clinical Investigation, Vol. 112, No. 3, (August 2003), p. 379 - 388 (Reference 2) (submitted herewith) discusses the repression of glomerular nephritis by inhibition of ECM accumulation. Reference 2 shows that a mutant PAI-1 inhibits the accumulation of collagen, and alleviates the symptoms of glomerular nephritis in a glomerular nephritis animal model (anti-Thy-1 antibody model). See, Fig. 4, Fig. 6 c and d, Fig. 10, Collagen I of Reference 2. (Note that mutant PAI-1 is a protein where the PAI-1 function has been destroyed and thus functions as a competitive inhibitor to the native PAI-1.)

On the basis of References 1 and 2, the two previously submitted *Shimizu, et al.* references, the previously submitted *Al-Bayati et al.* reference, descriptions in the specification, and the background art, it is clear that the inhibition of the over-production and accumulation of ECM alleviates the symptoms of the glomerular nephritis. This finding strongly and reasonably suggests that therapy and prevention are possible by the repression by galectin-3 inhibition of the over-production and accumulation of ECM.

Thus, the invention is enabled and the rejection should be removed.

Rejection Under 35 U.S.C. § 112, second paragraph

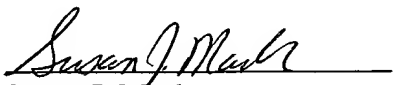
In paragraph No. 8 at page 9 of the Office Action, the Examiner rejected claims 25, 30, and 35 under 35 U.S.C. § 112, second paragraph, as being indefinite. In particular, the Examiner asserted that essential steps in the method for inhibiting diseases, i.e., the outcome of the process are omitted.

Claim 25 has been amended to recite the outcome. Therefore the rejection is overcome and should be removed.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860

WASHINGTON OFFICE
23373
CUSTOMER NUMBER

Susan J. Mack
Registration No. 30,951

Date: January 30, 2004